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BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Application Number: 10/582,499
Filing Date: June 09, 2006
Appellant(s): BRUECK-SCHEFFLER, ANTJE

Joshua Goldberg
Reg. No. 44,126
For Appellant

EXAMINER'S ANSWER

This is in response to the appeal brief filed August 8, 2011 appealing from the Office action mailed March 11, 2011.

The Examiner would like to bring to the attention of the Board and to all those concerned that a clerical error was made in the Final Rejection filed March 11, 2011. Specifically, claim 10 was not indicated in the heading of any of the rejections, but the limitation of claim 10 (wherein the excipient is a suspending agent) is addressed on page 3 of the Final office action, line 4 in the Nishibe et al. paragraph. Further, evidence of the clerical error can be evidenced by the following: 1) the Examiner indicated that claim 10 was rejected on the PTOL-326 form; 2) the Examiner indicated that all previous 35 U.S.C. 103(a) rejections made in the previous office action (the Non-Final filed on July 20, 1010) were upheld; and 3) in the Advisory Action filed July 7, 2011, the Examiner indicated that claim 10 was rejected on the PTOL-303 form and in the continuing comments on page 2, line 4. Thus, please view the 35 U.S.C. 103(a) rejection over Nishibe et al. in view of Saidi et al. and Lintz et al. to reject claims 1-4, 7-10 and 12-20. All rejections depending on this rejection should reflect the same correction.

(1) Real Party in Interest

The examiner has no comment on the statement, or lack of statement, identifying by name the real party in interest in the brief.

(2) Related Appeals and Interferences

The examiner is not aware of any related appeals, interferences, or judicial proceedings which will directly affect or be directly affected by or have a bearing on the Board's decision in the pending appeal.

(3) Status of Claims

The following is a list of claims that are rejected and pending in the application:

Claims 1-10 and 12-41 are pending. Claims 1-10 and 12-20 are rejected and on appeal. Claim 11 is cancelled. Claims 21-41 are withdrawn.

(4) Status of Amendments After Final

The examiner has no comment on the appellant's statement of the status of amendments after final rejection contained in the brief.

The examiner agrees that the amendments to the claims entered July 7, 2011 overcame the claim objection.

(5) Summary of Claimed Subject Matter

The examiner has no comment on the summary of claimed subject matter contained in the brief.

(6) Grounds of Rejection to be Reviewed on Appeal

The examiner has no comment on the appellant's statement of the grounds of rejection to be reviewed on appeal. Every ground of rejection set forth in the Office action from which the appeal is taken (as modified by any advisory actions) is being maintained by the examiner except for the grounds of rejection (if any) listed under the subheading "WITHDRAWN REJECTIONS." New grounds of rejection (if any) are provided under the subheading "NEW GROUNDS OF REJECTION."

(7) Claims Appendix

The examiner has no comment on the copy of the appealed claims contained in the Appendix to the appellant's brief.

(8) Evidence Relied Upon

6,241,969 B1	Saidi et al.	06-2001
2006/0166953 A1	Nishibe et al.	07-2006
2004/0247628 A1	Lintz et al.	12-2004
2005/0175526 A1	Sambuco et al.	08-2005

Allen et al. "Inhaled corticosteroids: past lessons and future issues", Supplement to The Journal of Allergy and Clinical Immunology, Sept 2003, vol. 112, no. 3, pp. S1-S40

ACS Registry, Feb 1995, pg 1.

(9) Grounds of Rejection

The following ground(s) of rejection are applicable to the appealed claims:

Claims 1-4, 7-9 and 11-20 are rejected under 35 U.S.C. 103(a) as being unpatentable over Nishibe et al. in view of Saidi et al. and Lintz et al.

Nishibe et al. teach a ciclesonide containing sterile aqueous suspension sterilized by autoclaving (see abstract; addresses claims 1, 3 and 4). The suspension may comprise suspending agents and wetting agents such as hydroxypropylmethylcellulose (i.e. non-ionic excipients and suspending agent; see paragraphs 38 and 42; addresses claims 1, 9, 11 and 13). Ciclesonide is dispersed in an aqueous medium including the excipients (see page 3, paragraph 42, lines 5-8) to give a white uniform aqueous suspension before being autoclaved at 115 degrees C for 30 minutes, at 121 degrees C for 20 minutes or at 126 degrees C for 15 minutes (see page 3, paragraph 43 and 49; addresses claims 15-19).

Nishibe et al. does not specifically teach that the composition is suitable for nebulization (claim 1), nor that the composition comprises the specific non-ionic agent in claims 7 and 8. Nishibe et al. also does not teach specifically teach at least one non-ionic agent for adjusting osmolality (claims 1 and 2), nor the osmolality range in claim 20. Nishibe et al. does not specifically teach the motivation for the specific suspending agent polysorbate (claim 14), nor the pH modifying agents of claim 12.

Saidi et al. teach an aqueous composition to treat ailments and diseased of the respiratory tract, particularly the lungs, comprising a cortiscosteroid that can be delivered through a nebulizer (see abstract). The composition comprises an osmolality agent such as glucose such that the osmolality of the composition is from about 280-300 mosmol/kg (see column 7, lines 3-9; addresses claims 1, 7, 8 and 20). The composition also comprises a surfactant such as sorbitan esters (Tween series; i.e. polysorbate; see column 8, line 57; addresses claim 14).

Lintz et al. teach pharmaceutical kits for the preparation of liquid composition that are administered as aerosols through nebulization (see abstract and paragraph 18). Drugs to be delivered include ciclesonide (see paragraph 19) that can be administered with excipients such as citric and tartaric acid to adjust the pH (see paragraph 25) and surfactants to increase the wettability of the active compound or to improve the dissemination of the aerosol droplets in the lungs (see paragraph 27). Preferable surfactants include Tween 60 (i.e. polysorbate; see paragraph 27, last two lines).

To one of ordinary skill in the art at the time of the invention would have found it obvious and motivated to combine the method of Nishibe et al. and providing the composition in a nebulizer because Saidi et al. teach that compositions can be made with cortiscosteroids to be delivered through a nebulizer to provide treatment for ailments and diseases of the respiratory tract (see abstract).

To one of ordinary skill in the art at the time of the invention would have found it obvious and motivated to combine the method of Nishibe et al. and providing the osmolality agents of claims 1, 2, 7 and 8 and at the osmolality range of claim 20 because Saidi et al. teach nebulizer compositions comprising cortiscosteroids that have an osmolality agent such as glucose such that the osmolality of the composition is from about 280-300 mosmol/kg (see column 7, lines 3-9). Buffers may be used to adjust the pH (see column 6, lines 64-66).

To one of ordinary skill in the art at the time of the invention would have found it obvious and motivated to combine the method of Nishibe et al. in view of Saidi et al. and providing an organic acid of claim 12 as a pH modifying agent because Saidi et al. and Lintz et al. teach that nebulized composition of drugs such as ciclesonide can be administered with pH modifiers. Particularly, Lintz et al. teach that organic acids such as citric and tartaric acid to adjust the pH (see abstract and paragraphs 18, 19 and 25).

To one of ordinary skill in the art at the time of the invention would have found it obvious and motivated to combine the method of Nishibe et al. and providing the specific suspending agent polysorbate because Lintz et al. teach that nebulized composition of drugs such as ciclesonide can be administered with excipients such as surfactants to increase the wettability of the active compound or to improve the dissemination of the aerosol droplets in the lungs (see paragraph 27). Preferable surfactants include Tween 60 (i.e. polysorbate; see paragraph 27, last two lines).

In regards to claim 16, since Nisibe et al. adds ciclesonide to the non-ionic agent, it would be obvious to one skilled in the art to also add ciclesonide to the non-ionic agent Saidi et al. to adjust the osmolality.

Claim 5 is rejected under 35 U.S.C. 103(a) as being unpatentable over Nishibe et al. in view of Saidi et al. and Lintz et al. as applied to claims 1-4, 7-9 and 11-20, in further view of Allen et al. and ACS Registry.

The teachings of Nishibe et al., Saidi et al. and Lintz et al. are as taught above for claims 1-4, 7-9 and 11-20.

Nischibe et al., Saidi et al. and Lintz et al. do not teach the ciclesonide derivatives of claim 5.

Allen et al. teach that CIC-AP is the active metabolite of ciclesonide in the lungs (see figure 10).

ACS Registry identifies CIC-AP as 16α,17-(22R,S)-cyclohexylmethylene-dioxy-11β,21-dihydroxypregna-1,4-diene-3,20-dione, and as the active metabolite of ciclesonide.

To one of ordinary skill in the art at the time of the invention would have found it obvious and motivated to combine the method of Nishibe et al. in view of Saidi et al. and providing the ciclesonide derivatives of claim 5 because Allen et al. and the ACS registry identify 16α,17-(22R,S)-cyclohexylmethylene-dioxy-11β,21-dihydroxypregna-1,4-diene-3,20-dione as the active metabolite of ciclesonide (see page 1, paragraph 6).

Claim 6 is rejected under 35 U.S.C. 103(a) as being unpatentable over Nishibe et al. in view of Saidi et al. and Lintz et al. as applied to claims 1-4, 7-9 and 11-20, in further view of Sambuco et al.

The teachings of Nishibe et al., Saidi et al. and Lintz et al. are as taught above for claims 1-4, 7-9 and 11-20.

Nischibe et al., Saidi et al. and Lintz et al. do not teach the particle size of ciclesonide as in claim 6.

Sambuco et al. teach an aqueous suspension of sterile micronized drug particles, particularly corticosteroids such as ciclesonide, administered by inhalation, which produces homogenous dispersions of particles characterized by optimal size and size distribution (see abstract and paragraph 29). The particles are preferably less than 7μm

(see paragraph 33), which can more easily dissolve in the lung fluids and penetrate into the cells in a better way, giving rise to a prolonged activity (see paragraph 39).

To one of ordinary skill in the art at the time of the invention would have found it obvious and motivated to combine the method of Nishibe et al. in view of Saidi et al. and providing the particle sizes of claim 6 because Sambuco et al. teach that particle sizes less than 7μm (see paragraph 33) can more easily dissolve in the lung fluids and penetrate into the cells in a better way, giving rise to a prolonged activity (see paragraph 39).

(10) Response to Argument

> The Appellant argues that claim 11 was rejected, but claim 11 is a canceled claim. Further, there is no record of claim 10 being rejected.

The Examiner has addressed this issue in the beginning of the Examiner's Answer and repeated below. The Examiner would like to bring to the attention of the Board and to all those concerned that a clerical error was made in the Final Rejection filed March 11, 2011. Specifically, claim 10 was not indicated in the heading of any of the rejections, but the limitation of claim 10 (wherein the excipient is a suspending agent) is addressed on page 3 of the Final office action, line 4 in the Nishibe et al. paragraph. Additionally, claim 11 should not be rejected because it was cancelled. Further, evidence of the clerical error can be evidenced by the following: 1) the

Examiner indicated that claim 10 was rejected on the PTOL-326 form; 2) the Examiner indicated that all previous 35 U.S.C. 103(a) rejections made in the previous office action (the Non-Final filed on July 20, 1010) were upheld; and 3) in the Advisory Action filed July 7, 2011, the Examiner indicated that claim 10 was rejected on the PTOL-303 form and in the continuing comments on page 2, line 4. Thus, please view the 35 U.S.C. 103(a) rejection over Nishibe et al. in view of Saidi et al. and Lintz et al. to reject claims 1-4, 7-10 and 12-20. All rejections depending on this rejection should reflect the same correction.

> The Appellant argues that there is no motivation to combine the Nishibe et al., Saidi et al. and Lintz et al. references and for one skilled in the art to choose only "non-ionic excipients" Particularly, the suspension that is taught by Nishibe et al. is not intended for inhalation or nebulization (see paragraph 46) and silent with regard to the osmolality of the suspensions or the fact that the suspension must be isosmotic to avoid irritation during administration through nebulization. Further, the Nishibe et al. reference is faced with the technical problem of providing a sterile aqueous ciclesonide suspension that does not suffer from clogging and a suspension that is suitable for nebulization, i.e. inhalative administration.

The Examiner disagrees because the motivation to combine the references is to make a sterile inhalation formulation of ciclesonide. First, Nishibe et al. provides the teaching of a method to sterilize a suspension of ciclesonide. Although the compositions of Nishibe et al. are not administered via inhalation or nebulization, Saidi et al. provides the motivation to make a nebulizer formulation of ciclesonide. Particularly, Saidi et al. teach that composition can be made with cortiscosteroids to be delivered through a nebulizer to provide treatment for aliments and diseases of the

respiratory tract (see abstract). Therefore to make a nebulizer formulation of ciclesonide, one can use the sterile formulation of Nishibe et al. and add the osmolality agent and surfactant of Saidi et al. Lintz et al. provides the teaching that nebulized compositions of drugs such as ciclesonide can be administered with excipients such as surfactants to increase the wettability of the active compound or to improve the dissemination of the aerosol droplets in the lungs (see paragraph 27). In regards to the technical problem, Nishibe et al. overcomes the problem by providing a uniform sterilized suspension (see paragraph 2). Further, Sambuco et al. is used to teach the importance of particle size when administering to the lungs, which is used to reject claim 6. The use of only non-ionic excipients will be addressed below

> The Saidi et al. and Lintz et al. references does not teach autoclaving, so the reference cannot provide any motivation to solve the technical problems associated with autoclaving. Further, the compositions of Saidi et al. are formulated such that they contain the corticosteroid active agents in a dissolved state. The claims are directed to preparing suspensions of ciclesonide sterilized through autoclaving suitable for nebulization. The Examiner offers absolutely no substance to demonstrate how or why the ordinary skilled artisan would be so motivated in view of the clearly deficient teachings of the prior art. Other than the Examiner's mere hindsight and conclusory assertion that sufficient motivation exists to combine the diverse teachings of these cited references, no such motivation exists with any reasonable expectation of success.

In response to applicant's argument that there is no teaching, suggestion, or motivation to combine the references, the examiner recognizes that obviousness may be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so

found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. See *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988), *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992), and *KSR International Co. v. Teleflex, Inc.*, 550 U.S. 398, 82 USPQ2d 1385 (2007). In this case, Nishibe et al. provides a suspension of ciclesonide that was sterilized by autoclave. The fact that it is known to provide cortiscosteroids in the form for nebulization. Particularly, Saidi et al. provides the motivation of how to nebulize a cortiscosteroid formulation by addition of an osmolality agent to treat ailments and disease of the respiratory tract. Thus the motivation to provide a nebulizable form of the Nishibe et al. composition is to provide treatment for respiratory tract ailments and diseases. The connection between Nishibe et al., Saidi et al. and Lintz et al. is the use of a cortiscosteroid, Nishibe et al. and Lintz et al. particularly teach the cortiscosteroid ciclesonide. In response to applicant's argument that the examiner's conclusion of obviousness is based upon improper hindsight reasoning, it must be recognized that any judgment on obviousness is in a sense necessarily a reconstruction based upon hindsight reasoning. But so long as it takes into account only knowledge which was within the level of ordinary skill at the time the claimed invention was made, and does not include knowledge gleaned only from the applicant's disclosure, such a reconstruction is proper. See *In re McLaughlin*, 443 F.2d 1392, 170 USPQ 209 (CCPA 1971).

> The Appellant further argues that there is no teaching in the Nishibe et al., Saidi et al., Lintz et al. and Sambuco references to select only non-ionic

> agents. Saidi et al. show very little difference between those solutions containing sodium chloride and those without sodium chloride (see example 5). Further, the amounts are not satisfactory. On the other hand the Applicants have demonstrated that suspensions containing ionic agents rendered large white agglomerates that would not be suitable for nebulization (see example 7 in specification). Further, Sambuco et al. and all other cited art does not address any of the technical problems associated with autoclaving, nor cure the deficiencies of Nishibe et al., Saidi et al. and Lintz et al. The Appellant is not simply attacking each reference individually but discussing the teachings of each reference in context of the teachings.

Again, the Examiner respectfully disagrees, and notes that one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.,* 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). The Examiner has already provided the connection between the cited references and why each reference is used. First, Saidi et al. is used to teach that non-ionic and ionic osmotic agents are known to be used in the art to adjust the osmolality of a composition from about 280-300 mosmol/kg for cortiscosteroid formulations (see column 7, lines 3-9). Nishibe et al, Saidi et al. and Lintz et al. disclose the use of cortiscosteroids, in which Nishibe et al. and Lintz et al. teach the use with ciclesonide. Second, example 5 of Saidi et al. does not use ciclesonide nor compare it with glucose so it cannot be compared. In regards to Appellant's Example 7, the tests are between a formulation comprising sodium chloride and another formulation not containing sodium chloride. This is not a true comparison with the closest art. The art (i.e. Saidi et al.) provides the teaching of an osmolality agent, particularly Saidi et al. provides glucose and sodium chloride (see column 7, lines 3-9). Third, one skilled in the art would have the ability

and skill to test for the best osmotic agent to render the best result for nebulization based on the teachings of Nishibe et al., Saidi et al., Lintz et al. and Sambuco et al. Selection of a known material based on its suitability for its intended use is obvious. Particularly, knowing the technical problem associated with autoclaving, Nishibe et al. provides a uniform suspension of ciclesonide and Saidi et al. provides the motivation and materials of providing a formulation such as Nishibe et al. in a nebulized form.

(11) Related Proceeding(s) Appendix

No decision rendered by a court or the Board is identified by the examiner in the Related Appeals and Interferences section of this examiner's answer.

For the above reasons, it is believed that the rejections should be sustained.

Respectfully submitted,

/KENDRA D CARTER/

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